

SEQUENCE LISTING

<120> Methods of Identifying Modulators of Bromodomains
<130> 2459-1-003

<140> 09/510,314 <141> 2000-02-22

<160> 44.

<170> PatentIn version 3.0

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Ser Leu Glu Lys Lys Pro Pro Phe Glu Lys Pro Ser Ile Glu Gln Gly 210 220
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2640

2700

2760

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2940

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3014

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any amino acid. One, two, or three may be missing.

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Pro Met Asp Leu Lys Thr Met Ser Glu Arg Leu Lys Asn Arg Tyr Tyr 50 55 60
Val Ser Lys Lys Leu Phe Met Ala Asp Leu Gln Arg Val Phe Thr Asn 65 70 75 80
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Pro Val Lys Lys Ser Glu Ala Pro Asp Tyr Tyr Glu Val Ile Arg Phe 35 40 45

Pro Ile Asp Leu Lys Thr Met Thr Glu Arg Leu Arg Ser Arg Tyr Tyr 50 55 60

Val Thr Arg Lys Leu Phe Val Ala Asp Leu Gln Arg Val Ile Ala Asn 65 70 75 80

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Ile Asp Ile Lys Ala Ile Glu Lys Lys Leu Gln Asn Asn Gln Tyr Val 50 60

Asp Lys Asp Gln Phe Ile Lys Asp Val Lys Arg Ile Phe Thr Asn Ala 65 70 75 80

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Pro Val Asp Pro Gln Leu Leu Gly Ile Pro Asp Tyr Phe Asp Ile Val Page 8

Lys Asn Pro Met Asp Leu Ser Thr Ile Lys Arg Lys Leu Asp Thr Gly Solution Signature Sig

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<213> Mus musculus

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Pro Met Asp Leu Gln Thr Leu Arg Glu Asn Val Arg Lys Arg Leu Tyr 50 60

Pro Ser Arg Glu Glu Phe Arg Glu His Leu Glu Leu Ile Val Lys Asn 70 75 80

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Ser Met Leu Asp Leu Cys Asp Glu Lys Leu Lys Glu Lys Glu 100 105 110

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35 40 45

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Pro Ser Arg Glu Glu Phe Arg Glu His Leu Glu Leu Ile Val Lys Asn 65 70 75 80

Ser Ala Thr Tyr Asn Gly Pro Lys His Ser Leu Thr Gln Ile Ser Gln 85 90 95

Ser Met Leu Asp Leu Cys Asp Glu Lys Leu Lys Glu Lys Glu Page 10

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His Pro Val Asn Lys Lys Phe Val Pro Asp Tyr Tyr Lys Val Ile Val 35 40 45

Asn Pro Met Asp Leu Glu Thr Ile Arg Lys Asn Ile Ser Lys His Lys 50 55 60

Tyr Gln Ser Arg Glu Ser Phe Leu Asp Asp Val Asn Leu Ile Leu Ala 65 70 75 80

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Ser Pro Met Asp Leu Glu Thr Ile Arg Lys Asn Ile Ser Lys His Lys 50 55 60

Tyr Gln Ser Arg Glu Ser Phe Leu Asp Asp Val Asn Leu Ile Leu Ala 65 70 75 80

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5 10 15

Met Lys Ala Leu Trp Lys His Gln Phe Ala Trp Pro Phe Arg Gln Pro 20 25 30

Val Asp Ala Val Lys Leu Gly Leu Pro Asp Tyr His Lys Ile Ile Lys 35 40 45

Gln Pro Met Asp Met Gly Thr Ile Lys Arg Arg Leu Glu Asn Asn Tyr 50 60

Tyr Trp Ala Ala Ser Glu Cys Met Gln Asp Phe Asn Thr Met Phe Thr 65 70 75 80

Asn Cys Tyr Ile Tyr Asn Lys Pro Thr Asp Asp Ile Val Leu Met Ala 85 90 95

Gln Thr Leu Glu Lys Ile Phe Leu Gln Lys Val Ala Ser Met Pro 100 105 110

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Val Asp Ala Ile Lys Leu Asn Leu Pro Asp Tyr His Lys Ile Ile Lys 35 40 45

Asn Pro Met Asp Met Gly Thr Ile Lys Lys Arg Leu Glu Asn Asn Tyr 50 60

Tyr Trp Ser Ala Ser Glu Cys Met Gln Asp Phe Asn Thr Met Phe Thr 65 70 75 80

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<213> Drosophila melanogaster

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Pro Val Lys Leu Asp Ile Pro Phe Tyr Phe Asn Tyr Ile Lys Arg Pro 35 40 45

Met Asp Leu Ser Thr Ile Glu Arg Lys Leu Asn Val Gly Ala Tyr Glu 50 60

Val Pro Glu Gln Ile Thr Glu Asp Phe Asn Leu Met Val Asn Asn Ser 65 70 75 80

Ile Lys Phe Asn Gly Pro Asn Ala Gly Ile Ser Gln Met Ala Arg Asn $85 \hspace{1cm} 90 \hspace{1cm} 95$

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<213> Homo sapiens

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Lys Pro Val Asp Ala Ser Ala Leu Gly Leu His Asp Tyr His Asp Ile 35 40 45

IleLysHisProMetAspLeuSerThrValLysArgLysMetGluAsnArgAspTyrArgAspAlaGlnGluPheAlaAlaAspValArgLeuMetPheSerAsnCysTyrLysTyrAsnProProAspHisAspValValAlaMetAlaArgLysLeuGlnAspValPheArgTyrAlaLysMet

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<213> Homo sapiens

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Lys Pro Val Asp Ala Glu Ala Leu Glu Leu His Asp Tyr His Asp Ile 35 40 45

Ile Lys His Pro Met Asp Leu Ser Thr Val Lys Arg Lys Met Asp Gly 50 60

Arg Glu Tyr Pro Asp Ala Gln Gly Phe Ala Ala Asp Val Arg Leu Met 65 70 75 80

Phe Ser Asn Cys Tyr Lys Tyr Asn Pro Pro Asp His Glu Val Val Ala 85 90 95

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Pro

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<213> Drosophila melanogaster

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Ile Lys Lys Pro Met Asp Leu Gly Thr Val Lys Arg Lys Met Asp Asn Page 14

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Val Lys Glu Pro Met Asp Leu Gly Thr Ile Ala Lys Lys Leu Asn Asp 50 55 60

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<213> Homo sapiens

<400> 27

Met Glu Met Gln Leu Thr Pro Phe Leu Ile Leu Leu Arg Lys Thr Leu $10 \,$ 15

Glu Gln Leu Gln Glu Lys Asp Thr Gly Asn Ile Phe Ser Glu Pro Val 20 25 30

Pro Leu Ser Glu Val Pro Asp Tyr Leu Asp His Ile Lys Lys Pro Met 35 40 45

Asp Phe Phe Thr Met Lys Gln Asn Leu Glu Ala Tyr Arg Tyr Leu Asn 50 60

Phe Asp Asp Phe Glu Glu Asp Phe Asn Leu Ile Val Ser Asn Cys Leu 80

Lys Tyr Asn Ala Lys Asp Thr Ile Phe Tyr Arg Ala Ala Val Arg Leu 95

Arg Glu Gln Gly Gly Ala Val Val Arg Gln Ala Arg 105

<210> 28 <211> 113 <212> PRT <213> Homo sar

<213> Homo sapiens

<400> 28

Ser Glu Asp Gln Glu Ala Ile Gln Ala Gln Lys Ile Trp Lys Lys Ala Ile Met Leu Val Trp Arg Ala Ala Ala Ala Asn His Arg Tyr Ala Asn Val Ala Leu Gln Pro Val Thr Asp Asp Ile Ala Pro Gly Tyr His Ser Ile Val Gln Arg Pro Met Asp Leu Ser Thr Ile Lys Lys Asn Ile Glu Asn Gly Leu Ile Arg Ser Thr Ala Glu Phe Gln Arg Asp Ile Met Leu Met 80 Phe Gln Asn Ala Val Met Tyr Asn Ser Ser Asp His Asp Val Tyr His Met Ala Val Glu Met Gln Arg Asp Val Leu Glu Gln Ile Gln Gln Phe

Leu

<210> 29 <211> 106 <212> PRT <213> Gallus gallus <400> 29

Asn Leu Pro Thr Val Asp Pro Ile Ala Val Cys His Glu Leu Tyr Asn Thr Ile Arg Asp Tyr Lys Asp Glu Gln Gly Arg Leu Leu Cys Glu Leu Phe Ile Arg Ala Pro Lys Arg Arg Asn Gln Pro Asp Tyr Tyr Glu Val Val Sor Gln Pro Ile Asp Leu Met Lys Ile Gln Gln Lys Leu Lys Met Glu Glu Tyr Asp Asp Val Asn Val Leu Thr Ala Asp Phe Gln Leu Leu 80 Phe Asn Asn Ala Lys Ala Tyr Tyr Lys Pro Asp Ser Pro Glu Tyr Lys

90

Ala Ala Cys Lys Leu Trp Glu Leu Tyr Leu 100 105

<210> 30

<211> 112

<212> PRT

<213> Gallus gallus

<400> 30

Ser Ser Pro Gly Tyr Leu Lys Glu Ile Leu Glu Gln Leu Leu Glu Ala 1 10 15

Val Ala Val Ala Thr Asn Pro Ser Gly Arg Leu Ile Ser Glu Leu Phe 20 25 30

Gln Lys Leu Pro Ser Lys Val Gln Tyr Pro Asp Tyr Tyr Ala Ile Ile 35 40 45

Lys Glu Pro Ile Asp Leu Lys Thr Ile Ala Gln Arg Ile Gln Asn Gly 50 60

Thr Tyr Lys Ser Ile His Ala Met Ala Lys Asp Ile Asp Leu Leu Ala 65 70 75 80

Lys Asn Ala Lys Thr Tyr Asn Glu Pro Gly Ser Gln Val Phe Lys Asp 85 90 95

Ala Asn Ala Ile Lys Lys Ile Phe Asn Met Lys Lys Ala Glu Ile Glu 100 105 110

<210> 31

<211> 112

<212> PRT

<213> Gallus gallus

<400> 31

Thr Ser Phe Met Asp Thr Ser Asn Pro Leu Tyr Gln Leu Tyr Asp Thr $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Val Arg Ser Cys Arg Asn Asn Gln Gly Gln Leu Ile Ser Glu Pro Phe 20 25 30

Phe Gln Leu Pro Ser Lys Lys Lys Tyr Pro Asp Tyr Tyr Gln Gln Ile 35 40 45

Lys Thr Pro Ile Ser Leu Gln Gln Ile Arg Ala Lys Leu Lys Asn His 50 60

Glu Tyr Glu Thr Leu Asp Gln Leu Glu Ala Asp Leu Asn Leu Met Phe 70 75 80

Glu Asn Ala Lys Arg Tyr Asn Val Pro Asn Ser Ala Ile Tyr Lys Arg 85 90 95

Val Leu Lys Met Gln Gln Val Met Gln Ala Lys Lys Glu Leu Ala 100 105 110

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<210>
         32
<211>
         113
<212>
<213>
         Gallus gallus
<400>
          32
Ser Lys Lys Asn Met Arg Lys Gln Arg Met Lys Ile Leu Tyr Asn Ala 1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15
Val Leu Glu Ala Arg Glu Ser Gly Thr Gln Arg Arg Leu Cys Asp Leu
20 25 30
```

Phe Met Val Lys Pro Ser Lys Lys Asp Tyr Pro Asp Tyr Tyr Lys Ile 35 40 45Ile Leu Glu Pro Met Asp Leu Lys Met Ile Glu His Asn Ile Arg Asn 50 55 60 Asp Lys Tyr Val Gly Glu Glu Ala Met Ile Asp Asp Met Lys Leu Met 65 70 75 80 Phe Arg Asn Ala Arg His Tyr Asn Glu Glu Gly Ser Gln Val Tyr Asn 85 90 95

Asp Ala His Met Leu Glu Lys Ile Leu Lys Glu Lys Arg Lys Glu Leu 100 105 110

Gly

<210> 33 115 <211> <212> PRT <213> Gallus gallus <400>

Lys Lys Ser Lys Tyr Met Thr Pro Met Gln Gln Lys Leu Asn Glu Val 1 5 10 15

Tyr Glu Ala Val Lys Asn Tyr Thr Asp Lys Arg Gly Arg Arg Leu Ser 20 25 30

Ala Ile Phe Leu Arg Leu Pro Ser Arg Ser Glu Leu Pro Asp Tyr Tyr 35 40 45

Met Ala Asn Lys Tyr Gln Asp Ile Asp Ser Met Val Glu Asp Phe Val 65 70 75 80

Met Met Phe Asn Asn Ala Cys Thr Tyr Asn Glu Pro Glu Ser Leu Ile 85 90 95

Tyr Lys Asp Ala Leu Val Leu His Lys Val Leu Leu Glu Thr Arg Arg 100 105 110

Glu Ile Glu 115

<210> 34

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        112
<212>
        PRT
<213>
        Description of unknown organism, see Jeanmougin et al.,
          Trends in Biochem. Sci. 22:151-153 (1997)
<400>
His Asn Ala Pro Phe Asp Lys Thr Lys Phe Asp Glu Val Leu Glu Ala
Leu Val Gly Leu Lys Asp Asn Glu Gly Asn Pro Phe Asp Asp Ile Phe 20 25 30
Glu Glu Leu Pro Ser Lys Arg Tyr Phe Pro Asp Tyr Tyr Gln Ile Ile 35 40 45
Gln Lys Pro Ile Cys Tyr Lys Met Met Arg Asn Lys Ala Lys Thr Gly
50 60
Lys Tyr Leu Ser Met Gly Asp Phe Tyr Asp Asp Ile Arg Leu Met Val 65 70 75 80
Ser Asn Ala Gln Thr Tyr Asn Met Pro Gly Ser Leu Val Tyr Glu Cys
85 90 95
Ser Val Leu Ile Ala Asn Thr Ala Asn Ser Leu Glu Ser Lys Asp Gly 100 105 110
<210>
        35
        113
<211>
<212>
        PRT
<213>
        Description of unknown organism, see Jeanmougin et al.,
          Trends in Biochem. Sci. 22:151-153 (1997)
<400>
        35
Gly Thr Asn Glu Ile Asp Val Pro Lys Val Ile Gln Asn Ile Leu Asp 1 5 10 15
Ala Leu His Glu Glu Lys Asp Glu Gln Gly Arg Phe Leu Ile Asp Ile 20 25 30
Phe Ile Asp Leu Pro Ser Lys Arg Leu Tyr Pro Asp Tyr Tyr Glu Ile 35 40 45
Ile Lys Ser Pro Met Thr Ile Lys Met Leu Glu Lys Arg Phe Lys Lys 50 60
Gly Glu Tyr Thr Thr Leu Glu Ser Phe Val Lys Asp Leu Asn Gln Met 65 70 75 80
Phe Ile Asn Ala Lys Thr Tyr Asn Ala Pro Gly Ser Phe Val Tyr Glu
85 90 95
Asp Ala Glu Lys Leu Ser Gln Leu Ser Ser Ser Leu Ile Ser Ser Phe 100 \hspace{1cm} 105 \hspace{1cm} 110
Ser
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<210> 36 <211> 113 <212> PRT

<213> Homo sapiens

<400> 36

Gly Thr Asn Glu Ile Asp Val Pro Lys Val Ile Gln Asn Ile Leu Asp Asp Ala Leu His Glu Glu Lys Asp Glu Gln Gly Arg Phe Leu Ile Asp Ile Phe Ile Asp Leu Pro Ser Lys Arg Leu Tyr Pro Asp Tyr Tyr Glu Ile Lys Ser Pro Met Thr Ile Lys Met Leu Glu Lys Arg Phe Lys Lys Gly Glu Tyr Thr Thr Leu Glu Ser Phe Val Lys Asp Leu Asn Gln Met 80 Phe Ile Asn Ala Lys Thr Tyr Asn Ala Pro Gly Ser Phe Val Tyr Glu 95

Asp Ala Glu Lys Leu Ser Gln Leu Ser Ser Ser Leu Ile Ser Ser Phe 100 105 110

Ser

<210> 37

<211> 114 <212> PRT

<213> Homo sapiens

<400> 37

Ser Pro Asn Pro Pro Asn Leu Thr Lys Lys Met Lys Lys Ile Val Asp $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Ala Val Ile Lys Tyr Lys Asp Ser Ser Ser Gly Arg Gln Leu Ser Glu 20 25 30

Val Phe Ile Gln Leu Pro Ser Arg Lys Glu Leu Pro Glu Tyr Tyr Glu 35 40 45

Leu Ile Arg Lys Pro Val Asp Phe Lys Lys Ile Lys Glu Arg Ile Arg 50 60

Asn His Lys Tyr Arg Ser Leu Asn Asp Leu Glu Lys Asp Val Met Leu 65 70 75 80

Leu Cys Gln Asn Ala Gln Thr Phe Asn Leu Glu Gly Ser Leu Ile Tyr 85 90 95

Glu Asp Ser Ile Val Leu Gln Ser Val Phe Thr Ser Val Arg Gln Lys 100 105 110

Ile Glu

<210> 38

<211> 113

<212> PRT <213> Gallus gallus

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<400> 38
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Ser Pro Asn Pro Pro Lys Leu Thr Lys Gln Met Asn Ala Ile Ile Asp Asp Thr Val Ile Asn Tyr Lys Asp Ser Ser Gly Arg Gln Leu Ser Glu Val Phe Ile Gln Leu Pro Ser Arg Lys Glu Leu Pro Glu Tyr Tyr Glu Leu Arg Sor Sor Sor Val Asp Phe Lys Lys Ile Lys Glu Arg Ile Arg Asn His Lys Tyr Arg Ser Leu Gly Asp Leu Glu Lys Asp Val Met Leu Leu Sor Cys His Asn Ala Gln Thr Phe Asn Leu Glu Gly Ser Gln Ile Tyr Glu Asp Ser Ile Val Leu Gln Ser Val Phe Lys Ser Ala Arg Gln Lys Ile Ala

<210> 39 <211> 114 <212> PRT <213> Gallus gallus

<400> 39

SerProAsnProProAsnLeuThrLysLysMetLysLysLysIleValAspAlaValIleLysTyrLysAspSerSerSerGlyArgGlnLeuSerGluValPheIleAspAspLysGluLeuProGluTyrTyrTyrGluLeuIleArgLysProValAspPheLysLysIleLysGluArgIleArgAsnHisLysTyrArgSerLeuAsnAspLeuGluLysAspValMetLeuGluAspSerIleValLeuGlnThrPheAsnLeuGluValArgGlnLysGluAspSerIleValLeuGlnSerValPheThrSerValArgGlnLys

Ile Glu

<210> 40 <211> 105 <212> PRT <213> Homo sapiens <400> 40 Ala Leu Phe Cys His Glu Pro Cys Arg Pro Leu His Gln Leu Ala Thr Arg Met Asn Gln Arg Lys Cys Glu Arg Val Leu Leu Leu 11

Ala Leu Phe Cys His Glu Pro Cys Arg Pro Leu His Gln Leu Ala Thr 30

Asp Ser Thr Phe Ser Leu Asp Gln Pro Gly Gly Thr Leu Asp Leu Thr 45

Leu Ile Arg Ala Arg Leu Gln Glu Lys Leu Ser Pro Pro Tyr Ser Ser 60

Pro Gln Glu Phe Ala Gln Asp Val Gly Arg Met Phe Lys Gln Phe Asn 80

Lys Leu Thr Glu Asp Lys Ala Asp Val Gln Ser Ile Ile Gly Leu Gln 90

Arg Phe Phe Glu Thr Arg Met Asn Glu 105

<210> 41 <211> 105 <212> PRT <213> Mus musculus

<400> 41

Ala Leu Phe Cys His Glu Pro Cys Arg Pro Leu His Gln Leu Ala Thr Asp Ser Thr Phe Ser Met Glu Gln Pro Gly Gly Gly Thr Leu Asp Leu Thr Leu Gln Glu Pro Gly Gly Leu Ser Pro Pro Tyr Ser Ser Gln Glu Gln Glu Pro Gly Arg Met Pro Gly Gly Thr Leu Asp Leu Thr Glu Asp Lys Leu Thr Glu Asp Lys Ala Asp Val Gly Arg Met Phe Lys Gln Pro Asn 80 Lys Leu Thr Glu Asp Lys Ala Asp Val Gln Ser Ile Ile Gly Leu Gln Gln

<210> 42 <211> 108 <212> PRT <213> Mus sp. <400> 42

Arg Phe Phe Glu Thr Arg Met Asn Asp

100

Thr Lys Leu Thr Pro Ile Asp Lys Arg Lys Cys Glu Arg Leu Leu 15 10 15 Phe Leu Tyr Cys His Glu Met Ser Leu Ala Phe Gln Asp Pro Val Pro $\frac{1}{20}$

Leu Thr Val Pro Asp Tyr Tyr Lys Ile Ile Lys Asn Pro Met Asp Leu Ser Thr Ile Lys Lys Arg Leu Gln Glu Asp Tyr Cys Met Tyr Thr Lys Pro Glu Asp Phe Val Ala Asp Phe Arg Leu Ile Phe Gln Asn Cys Ala 65 70 75 80 Glu Phe Asn Glu Pro Asp Ser Glu Val Ala Asn Ala Gly Ile Lys Leu Glu Ser Tyr Phe Glu Glu Leu Leu Lys Asn Leu Tyr <210> 43 <211> 18 <212> PRT <213> Artificial Sequence <220> <223> synthetic bromodomain peptide <220> <221> Xaa <222> (1)..(1)<223> Xaa can be any single amino acid <220> <221> Xaa <222> (2)..(2)<223> Xaa can be any single amino acid <220> <221> Xaa <222> (4)..(6)<223> Xaa is a maximum of three amino acids. Each of these can be any amino acid. One may be missing. <220> <221> Xaa <222> (6)..(13)<223> Xaa is a maximum of eight amino acids. Each of these can be any amino acid. One, two, or three may be missing. <220> <221> xaa <222> (7)..(7)Xaa is a single amino acid that can be Pro, Lys, or His. <220> <221> Xaa <222> (8)..(8)Xaa is a single amino acid that can be any amino acid. <220> <221> xaa <222> (10)..(10)<223> Xaa is a single amino acid that can be a Tyr, Phe, or His.

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<220>
<221>
        Xaa
<222>
        (11) ... (15)
<223>
        Xaa is any amino acid.
<220>
<221> Xaa
<222> (17)..(17)
<223> Xaa is a
       Xaa is a single amino acid that can be Met, Ile, or Val.
<400> 43
Xaa Xaa Phe Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asp 1 10 15
       44
20
<210>
<211>
<212>
        PRT
<213>
        Artificial Sequence
<220>
<223>
        synthetic bromodomain peptide
<400> 44
Trp Pro Phe Met Glu Pro Val Lys Arg Thr Glu Ala Pro Gly Tyr Tyr 1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15
Glu Val Ile Arg
20
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